

=> fil reg

FILE 'REGISTRY' ENTERED AT 10:48:11 ON 27 AUG 2003

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 AUG 2003 HIGHEST RN 573649-48-6

DICTIONARY FILE UPDATES: 25 AUG 2003 HIGHEST RN 573649-48-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

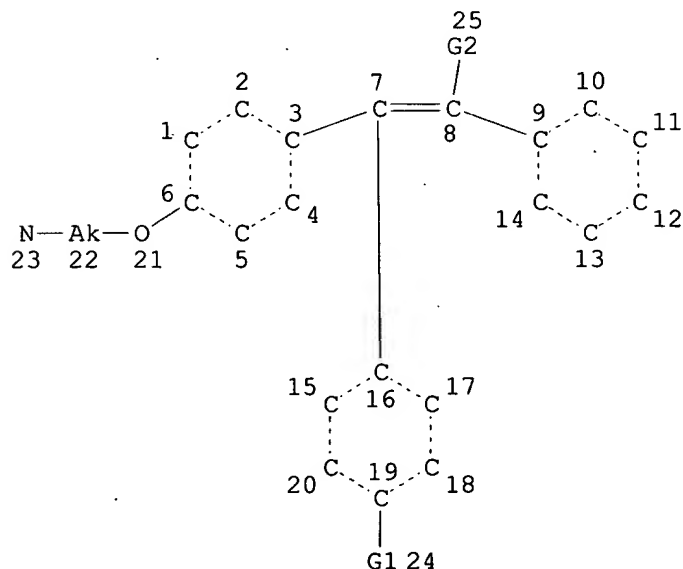
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que 120

L12 STR



Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
[jan.delaval@uspto.gov](mailto:jan.delaval@uspto.gov)

VAR G1=H/OH

VAR G2=H/AK

NODE ATTRIBUTES:

NSPEC IS RC AT 23

CONNECT IS M1 RC AT 10

CONNECT IS M1 RC AT 11

CONNECT IS M1 RC AT 12

CONNECT IS M1 RC AT 13

CONNECT IS M1 RC AT 14

CONNECT IS M1 RC AT 23

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

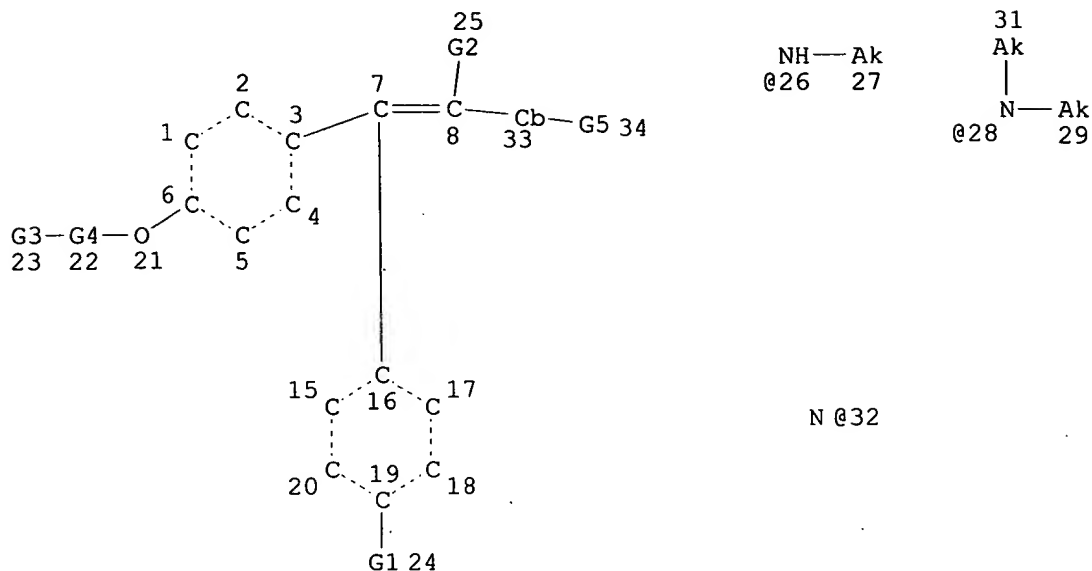
NUMBER OF NODES IS 25

STEREO ATTRIBUTES: NONE

L14 SCR 2039 OR 2043 OR 2054

L16 422 SEA FILE=REGISTRY CSS FUL L12 NOT L14

L17 STR



VAR G1=H/OH

VAR G2=H/AK

VAR G3=26/28/32

REP G4=(2-2) CH2

VAR G5=H/X/OH/AK

NODE ATTRIBUTES:

NSPEC IS R AT 32

CONNECT IS M1 RC AT 32

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 27.

STEREO ATTRIBUTES: NONE

L20 235 SEA FILE=REGISTRY SUB=L16 CSS FUL L17

100.0% PROCESSED 421 ITERATIONS

235 ANSWERS

SEARCH TIME: 00.00.01

=> d his

(FILE 'HOME' ENTERED AT 09:47:43 ON 27 AUG 2003)

SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:48:08 ON 27 AUG 2003

L1 2 S US20020065325/PN OR (WO2002-US26120# OR WO2000-US4892# OR US2  
SEL RN

FILE 'REGISTRY' ENTERED AT 09:50:12 ON 27 AUG 2003

L2 17 S E1-E17

L3 1 S L2 AND C26H29NO

L4 109 S C26H29NO/MF AND 46.150.18/RID AND 3/NR  
L5 24 S L4 AND BUTEN? AND PHENOXY AND DIMETHYL AND ETHANAMINE  
L6 5 S L5 NOT (LABELED OR (D OR T)/ELS OR 14C#)  
L7 4 S L6 NOT 2 BUTENYL  
L8 4 S L3,L7  
SEL RN  
L9 24 S E18-E21/CRN  
L10 14 S L9 NOT (COMPD OR WITH OR MXS/CI)  
L11 18 S L8,L10  
L12 STR  
L13 18 S L12 CSS SAM  
L14 SCR 2039 OR 2043 OR 2054  
L15 16 S L12 NOT L14 CSS  
L16 422 S L12 NOT L14 CSS FUL  
SAV L16 JKIM930/A  
STR L12  
L17 11 S L17 CSS SAM SUB=L16  
L18 4 S L16 AND C6-C6/ES  
L19 235 S L17 CSS FUL SUB=L16  
L20 SAV L20 JKIM930A/A  
L21 182 S L20 AND 3/NR  
L22 35 S L20 AND 4/NR  
L23 18 S L20 NOT L11,L21,L22  
L24 9 S L23 NOT (NC5/ES OR CLO4 OR MXS/CI OR C60H66N4O4 OR C20H8BR4O5)

FILE 'HCAPLUS' ENTERED AT 10:14:03 ON 27 AUG 2003

L25 5223 S L11  
L26 7288 S TAMOXIFEN# OR ICI47699 OR ICI() (47699 OR 47 699)  
L27 5795 S L19 OR L21 OR L22 OR L24  
L28 7816 S L25-L27  
E BLOOD VESSEL/CT  
L29 65303 S E3-E59  
L30 13171 S E60-E96  
L31 6190 S E109-E115  
E E3+ALL  
L32 143069 S E5,E4+NT  
E E25+ALL  
L33 92479 S E4,E5,E3+NT  
E E114+ALL  
E E28+ALL  
L34 4260 S E3  
E E8+ALL  
E E30+ALL  
L35 5383 S E3  
E E10+ALL  
L36 9115 S E4  
E IMPOTENCE/CT  
E E3+ALL  
L37 1385 S E2  
E ERECT/CT  
E E10+ALL  
E PENI/CT  
E PENIL/CT  
E E7+ALL  
L38 446 S E2  
E PENIS/CT  
L39 1507 S E3-E8  
E E3+ALL  
L40 1902 S E6+NT  
L41 324 S L28 AND L29-L40  
L42 177 S L41 AND (PD<=19990226 OR PRD<=19990226 OR AD<=19990226)  
L43 121 S L42 AND L25  
L44 125 S L42 AND L27

L45 125 S L43,L44  
L46 52 S L42 NOT L45  
L47 2 S L46 AND (NOREPINEPHRIN? OR CARDIOVASCULAR PATHOLOG?)/TI  
E LAMB F/AU  
L48 7 S E3,E11  
L49 22 S E29,E31  
E SCHUTTE B/AU  
L50 57 S E3,E4,E7-E9  
E YANG B/AU  
L51 787 S E3-E24  
E YANG BAO/AU  
L52 18 S E3  
L53 21 S E60  
L54 4 S L28 AND L48-L53  
L55 92 S L45 AND (PHARMACOL? OR PHARMACEUT?)/SC,SX  
L56 2386 S (L11 OR L19 OR L21 OR L22 OR L24) (L)THU/RL  
L57 551 S (L11 OR L19 OR L21 OR L22 OR L24) (L) (DMA OR PAC OR PKT)/RL  
L58 2620 S (L11 OR L19 OR L21 OR L22 OR L24) (L) (BAC OR BCP OR BPR OR BSU  
L59 104 S L45 AND L56-L58  
L60 119 S L55,L59  
L61 6 S L45 NOT L60  
SEL L60 DN AN 3 8 9 27 74 81 93 119  
L62 8 S L60 AND E1-E24  
L63 11 S L1,L47,L54,L62 AND L25-L62  
L64 4 S L63 AND (CL OR CL3 OR CLC3) (L)CHANNEL?  
L65 3 S L63 AND (CHANNEL OR ION OR CHLORIDE OR CHLORIN?) (L)BLOCK?  
L66 4 S L64,L65  
L67 4 S L63 AND CHLORIDE (L)CHANNEL  
L68 4 S L66,L67

FILE 'REGISTRY' ENTERED AT 10:43:58 ON 27 AUG 2003

L69 1 S NOREPINEPHRINE/CN  
L70 5 S C8H11NO3/MF AND NOREPINEPHRIN?  
L71 3 S L70 NOT LABELED  
L72 3 S L69,L71

FILE 'HCAPLUS' ENTERED AT 10:45:21 ON 27 AUG 2003

L73 27 S L72 AND L28  
L74 19 S NOREPINEPHRIN? AND L28  
L75 10 S L73,L74 AND L42  
SEL DN AN 3 5 8 9 10  
L76 5 S L75 NOT E25-E39  
L77 6 S L68,L76  
L78 6 S L63 NOT L77  
L79 12 S L77,L78 AND L1,L25-L68,L73-L78

FILE 'REGISTRY' ENTERED AT 10:48:11 ON 27 AUG 2003

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 10:48:33 ON 27 AUG 2003  
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FILE COVERS 1907 - 27 Aug 2003 VOL 139 ISS 9  
FILE LAST UPDATED: 25 Aug 2003 (20030825/ED)

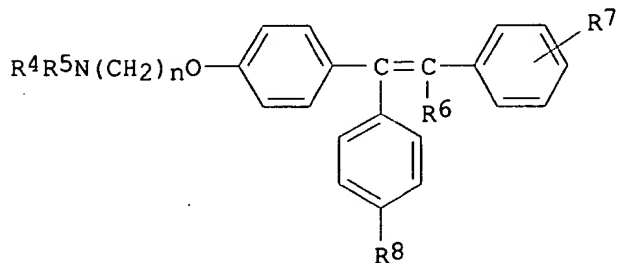
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 179 all hitstr tot

L79 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 2002:409273 HCAPLUS  
DN 137:722  
TI Use of CLC3 chloride channel  
blockers to modulate vascular tone  
IN Lamb, Fred S.; Schutte, Brian C.; Yang, Baoli  
PA USA  
SO U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U. S. Ser. No. 512,926.  
CODEN: USXXCO  
DT Patent  
LA English  
IC ICM A61K031-137  
ICS A61K031-55; A61K031-445; A61K031-40  
NCL 514651000  
CC 1-8 (Pharmacology)  
Section cross-reference(s): 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002065325	A1	20020530	US 2001-930105	20010815 <--
	WO 2003015614	A2	20030227	WO 2002-US26120	20020815 <--
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
	CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				
	GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				
	LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				
	PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				
	UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,				
	RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,				
	CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				
	PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,				
	NE, SN, TD, TG				
PRAI	US 1999-121727P	P	19990226	<--	
	US 2000-512926	A2	20000225	<--	
	US 2001-930105	A	20010815		
OS	MARPAT 137:722				
GI					



I

AB The invention discloses the use of chloride channel

**blocking** compd. I (R4= H, lower alkyl radical; R5= lower alkyl radical; or R4 and R5 connected with adjacent nitrogen to form a heterocyclic radical; R6= H, lower alkyl radical; R7=H, halogen, OH, lower alkyl radical, buta-1-3-dienyl radical which together with adjacent Ph forms a naphthyl radical; R8=H, OH; n=2) for the modulation of vascular tone in a patient having compromised vascular tissue. The present invention also provides methods for the modulation of vascular tone in a patient having compromised vascular tissue, with the administration of a **chloride channel blocking** agent or a pharmaceutically acceptable salt thereof.

- ST **chloride channel CLC3 blocker**  
blood vessel endothelium damage
- IT **Chloride channel**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CLC3; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Gene, animal  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(Clcn3; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Brain  
(cerebral cortex; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT **Ion channel blockers**  
(chloride; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT **Artery, disease**  
(coronary; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Nerve, disease  
Nerve, disease  
(death; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT **Blood vessel, disease**  
(endothelium, injury; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT **Blood vessel**  
(endothelium; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Neuroglia, disease  
(gliosis; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Brain  
(hippocampus; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT **Sexual behavior**  
(impotence; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Drug delivery systems  
(injections, i.v.; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Electric current  
(ionic, biol.; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Cell death  
Cell death  
(neuron; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT Drug delivery systems  
(oral; use of **CLC3 chloride channel blockers** to modulate vascular tone)
- IT **Artery, disease**

(restenosis; use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT Eye  
(retina; use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT Blood vessel  
(smooth muscle; use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT Antidiabetic agents  
Antihypertensives  
Diabetes insipidus  
Diabetes mellitus  
Human  
Hypertension  
Mammalia  
Mutation  
Seizures  
Surgery  
Vasoconstriction  
Vasodilators  
(use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT Estrogen receptors  
Glial fibrillary acidic protein  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT Penis  
(vascular, sympathetic tone; use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT 50-99-7, D-Glucose, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(tolerance; use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT 51-41-2, Norepinephrine 141436-78-4, Protein kinase C  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT 2149-70-4, Nitro-L-Arginine 21829-25-4, Nifedipine  
RL: PAC (Pharmacological activity); BIOL (Biological study)  
(use of **CLC3 chloride channel blockers** to modulate vascular tone)

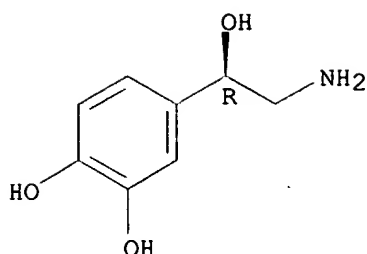
IT 61-68-7, Mefenamic acid 91-40-7 128-42-7, DNDS 530-78-9, Flufenamic acid 723-62-6, Anthracene-9-carboxylic acid 4394-00-7, Niflumic acid 10540-29-1, Tamoxifen 51023-76-8, SITS 53005-05-3, DIDS 53108-00-2, IAA-94 107254-86-4, NPPB  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(use of **CLC3 chloride channel blockers** to modulate vascular tone)

IT 51-41-2, Norepinephrine  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(use of **CLC3 chloride channel blockers** to modulate vascular tone)

RN 51-41-2 HCAPLUS

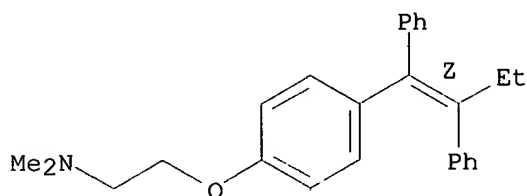
CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 10540-29-1, **Tamoxifen**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (use of **CLC3 chloride channel blockers** to modulate vascular tone)  
 RN 10540-29-1 HCAPLUS  
 CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.



L79 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2001:161506 HCAPLUS  
 DN 134:202697  
 TI Prevention and treatment of cardiovascular pathologies with  
**tamoxifen** analogues  
 IN Grainger, David J.; Metcalfe, James C.; Kunz, Lawrence L.; Schroff, Robert W.  
 PA NeoRx Corporation, USA  
 SO U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 478,936, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-445  
 ICS A61K031-40; A61K031-38; A61K031-135  
 NCL 514319000  
 CC 1-8 (Pharmacology)  
 FAN.CNT 14

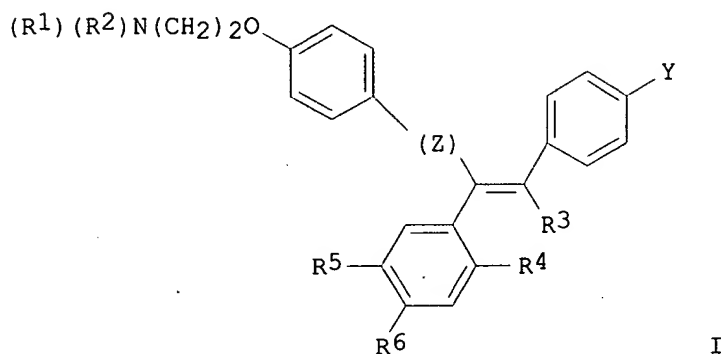
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6197789	B1	20010306	US 1997-973570	19971205 <--
	US 5595722	A	19970121	US 1995-476735	19950607 <--
	US 5770609	A	19980623	US 1995-486334	19950607 <--
	US 6395494	B1	20020528	US 1995-477393	19950607 <--
	WO 9640098	A2	19961219	WO 1996-US10211	19960607 <--
	WO 9640098	A3	19970619		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,



IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA  
 US 2002068731 A1 20020606 US 2001-754775 20010104 <--  
 PRAI US 1995-476735 A2 19950607 <--  
 US 1995-477393 A2 19950607 <--  
 US 1995-478936 B2 19950607 <--  
 US 1995-486334 A2 19950607 <--  
 WO 1996-US10211 W 19960607 <--  
 US 1993-11669 B2 19930128 <--  
 US 1993-61714 B2 19930513 <--  
 US 1993-62451 B2 19930513 <--  
 US 1994-241844 A2 19940512 <--  
 US 1994-242161 A2 19940512 <--  
 US 1997-973570 A1 19971205 <--  
 OS MARPAT 134:202697  
 GI



- AB A method for treating or preventing cardiovascular pathologies by administering a compd. of the formula (I): wherein Z is C:O or a covalent bond; Y is H or O(C1-C4)alkyl, R1 and R2 are individually (C1-C4)alkyl or together with N are a satd. heterocyclic group, R3 is Et or chloroethyl, R4 is H, R5 is I, O(C1-C4)alkyl or H and R6 is I, O(C1-C4)alkyl or H with the proviso that when R4, R5, and R6 are H, R3 is not ethyl; or a pharmaceutically acceptable salt thereof, effective to elevate the level of TGF-beta to treat and/or prevent conditions such as atherosclerosis, thrombosis, myocardial infarction, and stroke is provided. Useful compds. include idoxifene, toremifene or salts thereof. Further provided is a method for identifying an agent that elevates the level of TGF-beta. Another embodiment of the invention is an assay or kit to det. TGF-beta in vitro. Also provided is a therapeutic method comprising inhibiting smooth muscle cell proliferation assocd. with procedural vascular trauma employing the administration of **tamoxifen** or structural analogs thereof, including compds. of formula (I).
- ST **tamoxifen** analog cardiovascular pathol TGF beta; smooth muscle proliferation inhibition **tamoxifen** analog; thrombosis inhibition **tamoxifen** analog TGF beta; myocardial infarction treatment **tamoxifen** analog TGF; stroke treatment **tamoxifen** analog TGF beta
- IT Antiarteriosclerotics  
 (antiatherosclerotics; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Medical goods  
 (catheters, drug delivery with; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition

of vascular smooth muscle proliferation in relation to elevation of TGF beta)

- IT **Artery**  
(coronary, angioplasty, treatment of; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Cardiovascular system  
(disease; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Lipids, biological studies  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(metabolic disorders, treatment of cardiovascular pathol. in; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Cardiovascular agents  
Drug delivery systems  
(prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Proliferation inhibition  
(proliferation inhibitors; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT **Artery, disease**  
(restenosis, inhibition of; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT **Blood vessel**  
(smooth muscle; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT **Artery, disease**  
(stenosis, inhibition of; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Medical goods  
(stents, inhibition of restenosis from; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Diabetes mellitus  
(treatment of cardiovascular pathol. in; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT **Artery, disease**  
(treatment of; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT Transforming growth factors  
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)  
(.beta.-; prevention and treatment of cardiovascular pathol. with **tamoxifen** analogs and inhibition of vascular smooth muscle proliferation in relation to elevation of TGF beta)
- IT 10540-29-1D, **Tamoxifen**, analogs 82413-20-5,  
Droloxifene 84449-90-1, Raloxifene 89778-26-7, Toremifene

116057-66-0 116057-75-1, Idoxifene 116057-76-2

RL: BAC (Biological activity or effector, except adverse);  
 BSU (Biological study, unclassified); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)

(prevention and treatment of cardiovascular pathol. with  
 tamoxifen analogs and inhibition of vascular smooth muscle  
 proliferation in relation to elevation of TGF beta)

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE

- (1) Allen; US 2914563 1959 HCAPLUS
- (2) Anon; EP 0054168 1982 HCAPLUS
- (3) Anon; EP 054168 A1 1982 HCAPLUS
- (4) Anon; DE 4401554 1994 HCAPLUS
- (5) Anon; DE 4320896 1995 HCAPLUS
- (6) Anon; DE 4320898 1995 HCAPLUS
- (7) Anon; Drug & Market Development 1994, V5, P121
- (8) Anon; ICI Pharma 1992, P64033
- (9) Anon; The Breast Cancer Letter 1994, V20, P4
- (10) Crawley; US 4307111 1981 HCAPLUS
- (11) Dewald; US 3288806 1966 HCAPLUS
- (12) Elpern; US 3010965 1961
- (13) Fildes; US 4235988 1980 HCAPLUS
- (14) Harita; US 3940422 1976 HCAPLUS
- (15) Harita; US 4070484 1978
- (16) Harita; US Re32944 1989
- (17) Jones; US 4133814 1979 HCAPLUS
- (18) Jones; US 4418068 1983 HCAPLUS
- (19) Magarian; US 4442119 1984 HCAPLUS
- (20) Palopoli; US 3168565 1965 HCAPLUS
- (21) Palopoli; US 3634517 1972 HCAPLUS
- (22) Peters; US 4380635 1983 HCAPLUS
- (23) Sok, C; US 4093709 1978
- (24) Spears; US 4512762 1985
- (25) Speight, T; Avery's Drug Treatment-Principles and Practice of Clinical  
 Pharmacology and Therapeutics 1987, P594
- (26) Suarez; US 4230862 1980 HCAPLUS
- (27) Suarez; US 4323707 1982 HCAPLUS
- (28) Venton; US 4239778 1980 HCAPLUS

IT 10540-29-1D, Tamoxifen, analogs

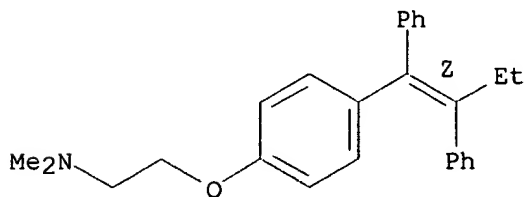
RL: BAC (Biological activity or effector, except adverse);  
 BSU (Biological study, unclassified); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)

(prevention and treatment of cardiovascular pathol. with  
 tamoxifen analogs and inhibition of vascular smooth muscle  
 proliferation in relation to elevation of TGF beta)

RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.



DN 133:172188  
 TI Methods to reduce the sensitivity of endothelially-compromised vascular smooth muscle  
 IN Lamb, Fred S.  
 PA University of Iowa Research Foundation, USA  
 SO PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC A61K031-00  
 CC 1-8 (Pharmacology)  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050023	A2	20000831	WO 2000-US4892	20000226 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-121727P	P	19990226 <--		
OS	MARPAT 133:172188				
AB	The present invention discloses materials and methods useful to treat sensitivity of endothelially-compromised vascular smooth muscle. In one embodiment, CLC3 blockers, particularly compds. of formula I are used to treat sensitivity.				
ST	vascular smooth muscle endothelial damage treatment <b>tamoxifen</b> ; CLC3 blocker vascular smooth muscle endothelial damage				
IT	<b>Chloride channel</b> RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (CLC-3; methods to reduce sensitivity of endothelially-compromised vascular smooth muscle using <b>CLC3 chloride channel blockers</b> such as <b>tamoxifen</b> in relation to use of other agents)				
IT	<b>Ion channel blockers</b> ( <b>chloride</b> , CLC-3; methods to reduce sensitivity of endothelially-compromised vascular smooth muscle using <b>CLC3 chloride channel blockers</b> such as <b>tamoxifen</b> in relation to use of other agents)				
IT	<b>Artery, disease</b> (coronary, restenosis, agents for treatment of; methods to reduce sensitivity of endothelially-compromised vascular smooth muscle using <b>CLC3 chloride channel blockers</b> such as <b>tamoxifen</b> in relation to use of other agents)				
IT	<b>Artery, disease</b> (coronary, vascular endothelial damage in, treatment of; methods to reduce sensitivity of endothelially-compromised vascular smooth muscle using <b>CLC3 chloride channel blockers</b> such as <b>tamoxifen</b> in relation to use of other agents)				
IT	<b>Blood vessel, disease</b> (diabetic angiopathy, treatment of; methods to reduce sensitivity of endothelially-compromised vascular smooth muscle using <b>CLC3 chloride channel blockers</b> such as <b>tamoxifen</b> in relation to use of other agents)				
IT	<b>Blood vessel, disease</b> (endothelium, injury; methods to reduce sensitivity				

of endothelially-compromised vascular **smooth muscle**  
 using **CLC3 chloride channel**  
**blockers** such as **tamoxifen** in relation to use of  
 other agents)

IT Antidiabetic agents

Antihypertensives

Drug interactions

**Vasodilators**

(methods to reduce sensitivity of endothelially-compromised vascular  
 smooth muscle using **CLC3 chloride channel**  
**blockers** such as **tamoxifen** in relation to use of  
 other agents)

IT **Blood vessel**

(**smooth muscle**; methods to reduce sensitivity of  
 endothelially-compromised vascular **smooth muscle**  
 using **CLC3 chloride channel**  
**blockers** such as **tamoxifen** in relation to use of  
 other agents)

IT Hypertension

Surgery

(vascular endothelial damage from, treatment of; methods to reduce  
 sensitivity of endothelially-compromised vascular smooth muscle using  
**CLC3 chloride channel blockers**  
 such as **tamoxifen** in relation to use of other agents)

IT 10540-29-1, **Tamoxifen**

RL: BAC (Biological activity or effector, except adverse);

BSU (Biological study, unclassified); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)

(methods to reduce sensitivity of endothelially-compromised vascular  
 smooth muscle using **CLC3 chloride channel**  
**blockers** such as **tamoxifen** in relation to use of  
 other agents)

IT 51-41-2, **Norepinephrine** 7447-40-7, Potassium

**chloride** (KCl), biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); BIOL (Biological study)

(vasoconstriction after endothelial damage from, normalization of;  
 methods to reduce sensitivity of endothelially-compromised vascular  
 smooth muscle using **CLC3 chloride channel**  
**blockers** such as **tamoxifen** in relation to use of  
 other agents)

IT 10540-29-1, **Tamoxifen**

RL: BAC (Biological activity or effector, except adverse);

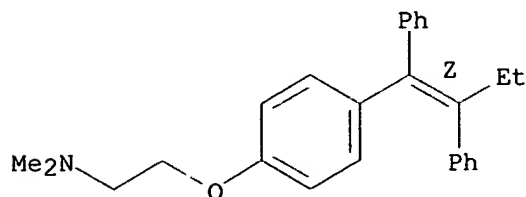
BSU (Biological study, unclassified); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)

(methods to reduce sensitivity of endothelially-compromised vascular  
 smooth muscle using **CLC3 chloride channel**  
**blockers** such as **tamoxifen** in relation to use of  
 other agents)

RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.



## IT 51-41-2, Norepinephrine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

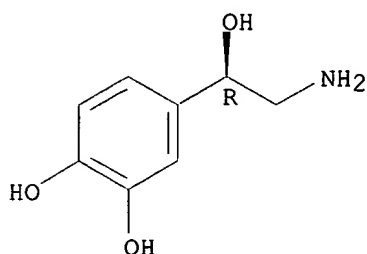
(vasoconstriction after endothelial damage from, normalization of; methods to reduce sensitivity of endothelially-compromised vascular smooth muscle using **CLC3 chloride channel**

**blockers** such as **tamoxifen** in relation to use of other agents)

RN 51-41-2 HCAPLUS

CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:392207 HCAPLUS

DN 133:117961

TI Endothelium modulates anion channel-dependent aortic contractions to iodide

AU **Lamb, Fred S.**; Barna, Thomas J.

CS Department of Pediatrics, University of Iowa, Iowa City, IA, 52242, USA

SO American Journal of Physiology (2000), 278(5, Pt. 2), H1527-H1536

CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society

DT Journal

LA English

CC 13-6 (Mammalian Biochemistry)

AB Anion currents contribute to vascular smooth muscle (VSM) membrane potential. The substitution of extracellular **chloride** (**Cl**) with iodide (I) or bromide (Br) initially inhibited and then potentiated isometric contractile responses of rat aortic rings to **norepinephrine**. Anion substitution alone produced a small relaxation, which occurred despite a lack of active tone and minimal subsequent contraction of endothelium-intact rings (4.2  $\pm$  1.2% of the response to 90 mM KCl). Endothelium-denuded rings underwent a similar initial relaxation but then contracted vigorously (I > Br). Responses to 130 mM I (93.7  $\pm$  1.9% of 90 mM KCl) were inhibited by nifedipine (10<sup>-6</sup> M), niflumic acid (10<sup>-5</sup> M), **tamoxifen** (10<sup>-5</sup> M), DIDS (10<sup>-4</sup> M), and HCO<sub>3</sub><sup>-</sup>-free buffer (HEPES 10 mM) but not by bumetanide (10<sup>-5</sup> M). Intact rings treated with N.omega.-nitro-L-arginine (10<sup>-4</sup> M) responded weakly to I (15.5  $\pm$  2.1% of 90 mM KCl), whereas Hb (10<sup>-5</sup> M), indomethacin (10<sup>-6</sup> M), 17-octadecynoic acid (10<sup>-5</sup> M), and 1H-[1,2,4]oxadiazole[4,3-a]quinoxalin-1-one (10<sup>-6</sup> M) all failed to augment the response of intact rings to I. We hypothesize that VSM takes up I primarily via an anion exchanger. Subsequent I efflux through anion **channels** having a selectivity of I > Br > Cl produces depolarization. In endothelium-denuded or agonist-stimulated vessels, this current is sufficient to activate voltage-dependent calcium **channels** and cause contraction. Neither nitric oxide nor prostaglandins are the primary endothelial modulator of these anion **channels**. If they are regulated by an endothelium-dependent

- hyperpolarizing factor it is not a cytochrome P 450 metabolite.
- ST iodide bromide anion **channel** vasoconstriction vascular smooth muscle; **chloride** calcium **channel** anion exchanger membrane depolarization iodide vasoconstriction; nitric oxide vascular endothelium iodide vasoconstriction
- IT **Artery**  
(aorta, endothelium; endothelium modulation of anion channel-dependent aortic contractions to iodide and bromide)
- IT Transport proteins  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(bicarbonate-**chloride**-exchanging; involvement of calcium and **chloride channels**, anion exchanger and membrane depolarization in anion **channel**-dependent aortic contractions to iodide and bromide)
- IT Membrane potential  
(biol.; involvement of calcium and **chloride channels**, anion exchanger and membrane depolarization in anion **channel**-dependent aortic contractions to iodide and bromide)
- IT Polarization  
(depolarization, biol.; involvement of calcium and **chloride channels**, anion exchanger and membrane depolarization in anion **channel**-dependent aortic contractions to iodide and bromide)
- IT **Vasoconstriction**  
**Vasodilation**  
(endothelium modulation of anion channel-dependent aortic contractions to iodide and bromide)
- IT Anion channel  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(endothelium modulation of anion channel-dependent aortic contractions to iodide and bromide)
- IT **Chloride channel**  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(involvement of calcium and **chloride channels**, anion exchanger and membrane depolarization in anion **channel**-dependent aortic contractions to iodide and bromide)
- IT Permeability  
(selective, of anion **channel** to I, Br, and Cl; endothelium modulation of anion **channel**-dependent aortic contractions to iodide and bromide)
- IT **Blood vessel**  
(smooth muscle; endothelium modulation of anion channel-dependent aortic contractions to iodide and bromide)
- IT Calcium **channel**  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(voltage-dependent; involvement of calcium and **chloride channels**, anion exchanger and membrane depolarization in anion **channel**-dependent aortic contractions to iodide and bromide)
- IT 20461-54-5, Iodide, biological studies 24959-67-9, Bromide, biological studies  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(endothelium modulation of anion channel-dependent aortic contractions to iodide and bromide)
- IT 10102-43-9, Nitric oxide, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(endothelium modulation of anion channel-dependent aortic contractions to iodide and bromide in relation to)

IT 16887-00-6, **Chloride**, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)  
(involvement of calcium and **chloride channels**,  
anion exchanger and membrane depolarization in anion **channel**  
-dependent aortic contractions to iodide and bromide).

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L79 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:782960 HCAPLUS

DN 132:384

TI **Tamoxifen** versus placebo in the treatment of peyronie's disease

AU Teloken, Claudio; Rhoden, Ernani Luis; Grazziotin, Tulio Meyer; Da Ros, Carlos Teodosio; Sogari, Paulo Roberto; Souto, Carlos Ary Vargas

CS Department of Urology, Andrology Section, Santa Casa Hospital and Fundacao Faculdade Federal de Ciencias Medicas, Alegre, Brazil

SO Journal of Urology (Baltimore) (1999), 162(6), 2003-2005

CODEN: JOURAA; ISSN: 0022-5347



PB Lippincott Williams & Wilkins

DT Journal

LA English

CC 1-12 (Pharmacology)

AB Purpose: We evaluated the effects of oral **tamoxifen** and placebo in patients with Peyronie's disease. Materials and Methods: We selected 25 patients with Peyronie's disease who did not have calcified plaque for treatment in the androl. outpatient clinic. A medical history was obtained, and phys. examn., penile x-ray, penile ultrasound and pharmacol. induced erection with prostaglandin E1 were performed. Patients were randomly divided into group 1-those who received 20 mg. **tamoxifen** twice daily for 3 mo and group 2-those who received placebo for the same period. The same evaluations were done 4 mo later and results were compared. Qual. (chi-square test) and quant. (Student's t test) results were analyzed using the Yates correction factor with  $p < 0.05$  considered significant. Results: Pain subsided in 66.6 and 75% of the patients treated with **tamoxifen** and placebo, resp. ( $p > 0.05$ ). In groups 1 and 2 a redn. in the penile deformity was noticed by 46.1 and 41.7% of the patients ( $p > 0.05$ ), and a decrease in plaque size was noticed by 30.7 and 25%, resp. On the other hand, objective measurements did not reveal any difference in plaque area or curvature angle. Conclusions: This study did not show significant improvement in pain, curvature or plaque size in patients with Peyronie's disease who were treated with **tamoxifen** compared with those treated with placebo.

ST **tamoxifen** peyronie disease sexual disorder penis

IT Sexual behavior

(disorder, penis; **tamoxifen** vs. placebo in treatment of peyronie's disease in humans)

IT **Penis**

(peyronie's disease; **tamoxifen** vs. placebo in treatment of peyronie's disease in humans)

IT 10540-29-1, **Tamoxifen**

RL: BAC (Biological activity or effector, except adverse);

BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**tamoxifen** vs. placebo in treatment of peyronie's disease in humans)

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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- (13) Ralph, D; J Urol 1996, V155, P159 MEDLINE
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IT 10540-29-1, **Tamoxifen**

RL: BAC (Biological activity or effector, except adverse);

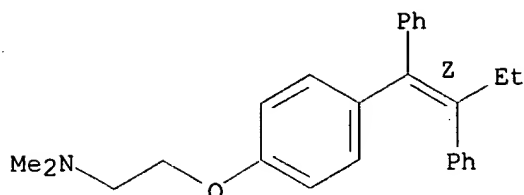
BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**tamoxifen** vs. placebo in treatment of peyronie's disease in humans)

RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



- L79 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1998:492891 HCAPLUS  
 DN 129:211974  
 TI Chloride ion currents contribute functionally to **norepinephrine**  
 -induced vascular contraction  
 AU **Lamb, Fred S.**; Barna, Thomas J.  
 CS Department of Pediatrics, University of Iowa, Iowa City, IA, 52242, USA  
 SO American Journal of Physiology (1998), 275(1, Pt. 2), H151-H160  
 CODEN: AJPHAP; ISSN: 0002-9513  
 PB American Physiological Society  
 DT Journal  
 LA English  
 CC 2-8 (Mammalian Hormones)  
 AB **Norepinephrine** (NE) increases **Cl<sup>-</sup>** efflux from vascular smooth muscle (VSM) cells. An increase in **Cl<sup>-</sup>** conductance produces membrane depolarization. The authors hypothesized that if **Cl<sup>-</sup>** currents are important for agonist-induced depolarization, then interfering with cellular **Cl<sup>-</sup>** handling should alter contractility. Isometric contraction of rat aortic rings was studied in a bicarbonate buffer. Substitution of extracellular **Cl<sup>-</sup>** with 130 mM methanesulfonate (MS; 8 mM **Cl<sup>-</sup>**) did not cause contraction. NE- and serotonin-induced contractions were potentiated in this low-**Cl<sup>-</sup>** buffer, whereas responses to K<sup>+</sup>, BAY K 8644, or NE in the absence of Ca<sup>2+</sup> were unaltered. Substitution of **Cl<sup>-</sup>** with I<sup>-</sup> or Br<sup>-</sup> suppressed responses to NE. Inhibition of **Cl<sup>-</sup>** transport with bumetanide (10<sup>-5</sup> M) or bicarbonate-free conditions (10 mM HEPES) inhibited NE- but not KCl-induced contraction. The **Cl<sup>-</sup>**-**channel blockers** DIDS (10<sup>-3</sup> M), anthracene-9-carboxylic acid (10<sup>-3</sup> M), and niflumic acid (10<sup>-5</sup> M) all inhibited NE-induced contraction, whereas **tamoxifen** (10<sup>-5</sup> M) did not. Finally, disruption of sarcoplasmic reticular function with cyclopiazonic acid (10<sup>-7</sup> M) or ryanodine (10<sup>-5</sup> M) prevented the increase in the peak response to NE produced by low-**Cl<sup>-</sup>** buffer. The authors conclude that a **Cl<sup>-</sup>** current with a permeability sequence of I<sup>-</sup> > Br<sup>-</sup> > **Cl<sup>-</sup>** > MS is crit. to agonist-induced contraction of VSM.  
 ST chloride current **norepinephrine** vasoconstriction  
 IT Biological transport  
 (channel-mediated; **chloride** ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)  
 IT Vasoconstriction  
 (chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)  
 IT Calcium channel  
 Chloride channel  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)  
 IT Biological transport  
 (cotransport, sodium-potassium-chloride; chloride ion currents

- contribute functionally to **norepinephrine**-induced vascular contraction in rats)
- IT Polarization  
(depolarization, biol.; chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)
- IT Endoplasmic reticulum  
(sarcoplasmic reticulum; chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)
- IT **Blood vessel**  
(**smooth muscle**; chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)
- IT 50-67-9, Serotonin, biological studies 51-41-2, **Norepinephrine**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)
- IT 7440-09-7, Potassium, biological studies 7440-23-5, Sodium, biological studies 7440-70-2, Calcium, biological studies 16887-00-6, Chloride, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)
- IT 7440-09-7, Potassium, biological studies 7440-23-5, Sodium, biological studies 7440-70-2, Calcium, biological studies 16887-00-6, Chloride, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(transport; chloride ion currents contribute functionally to **norepinephrine**-induced vascular contraction in rats)
- RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
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IT 51-41-2, **Norepinephrine**

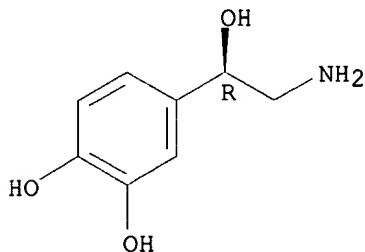
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(chloride ion currents contribute functionally to  
**norepinephrine**-induced vascular contraction in rats)

RN 51-41-2 HCAPLUS

CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1998:427775 HCAPLUS

DN 129:76502

TI Prevention and treatment of **cardiovascular pathologies**

IN Grainger, David J.; Metcalfe, James C.; Kunz, Lawrence L.; Schroff, Robert W.; Weissberg, Peter L.

PA NeoRx Corp., USA

SO U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 242,161.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-445

ICS A61K031-40; A61K031-38; A61K031-135

NCL 514319000

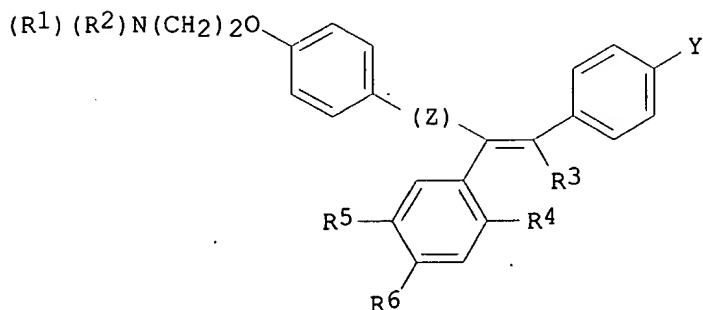
CC 1-8 (Pharmacology)

FAN.CNT 14

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5770609	A	19980623	US 1995-486334	19950607 <--
	US 5847007	A	19981208	US 1994-242161	19940512 <--
	US 5599844	A	19970204	US 1995-528810	19950915 <--
	US 5773479	A	19980630	US 1995-560808	19951121 <--
	CA 2223595	AA	19961219	CA 1996-2223595	19960607 <--
	WO 9640098	A2	19961219	WO 1996-US10211	19960607 <--
	WO 9640098	A3	19970619		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,

ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,  
 LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,  
 SE, SG  
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA  
 AU 9662773 A1 19961230 AU 1996-62773 19960607 <--  
 EP 833624 A2 19980408 EP 1996-921577 19960607 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI  
 JP 11510479 T2 19990914 JP 1996-502239 19960607 <--  
 US 5945456 A 19990831 US 1997-965254 19971106 <--  
 US 6197789 B1 20010306 US 1997-973570 19971205 <--  
 US 6251920 B1 20010626 US 1998-82643 19980521 <--  
 US 6262079 B1 20010717 US 1999-306606 19990506 <--  
 US 2002068731 A1 20020606 US 2001-754775 20010104 <--  
 PRAI US 1993-11669 B2 19930128 <--  
 US 1993-61714 B2 19930513 <--  
 US 1993-62451 B2 19930513 <--  
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 US 1995-560808 A1 19951121 <--  
 WO 1996-US10211 W 19960607 <--  
 US 1997-973570 A1 19971205 <--  
 US 1998-82643 A1 19980521 <--  
 OS MARPAT 129:76502  
 GI



AB A method for treating or preventing cardiovascular pathologies by administering I, wherein Z is CO or a covalent bond; Y is H or O(C1-C4)alkyl, R1 and R2 are individually (C1-C4)alkyl or together with N are a satd. heterocyclic group, R3 is Et or chloroethyl, R4 is H or together with R3 is -CH2CH2- or -S-, R5 is I, O(C1-C4)alkyl or H and R6 is I, O(C1-C4)alkyl or H with the proviso that when R4, R5, and R6 are H, R3 is not ethyl; or a pharmaceutically acceptable salt thereof, effective to activate or stimulate prodn. of TGF-beta to treat and/or prevent conditions such as atherosclerosis, thrombosis, myocardial infarction, and stroke is provided. Useful compds. include idoxifene and salts thereof. Further provided is a method for identifying a compd. that is a TGF-beta activator or prodn. stimulator is provided. Another embodiment of the invention is an assay or kit to det. TGF-beta in vitro. Also provided is a therapeutic method comprising inhibiting smooth muscle cell proliferation assocd. with procedural vascular trauma employing the

administration of **tamoxifen** or structural analogs thereof, including I. Some of the examples include impact of **tamoxifen** on vascular smooth muscle cells (VSMC) and the relationship to TGF-.beta. prodn. and activation and heparin effect on VSMC proliferation and differentiation.

ST TGFb prodn cardiovascular pathol

IT **Blood vessel**

Cell proliferation

(TGF-.beta. activators or prodn. stimulators in prevention and treatment of cardiovascular pathologies)

IT Cardiovascular system

(disease; TGF-.beta. activators or prodn. stimulators in prevention and treatment of cardiovascular pathologies)

IT **Blood vessel**

(**smooth muscle**; TGF-.beta. activators or prodn. stimulators in prevention and treatment of cardiovascular pathologies)

IT Transforming growth factors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(.beta.-; TGF-.beta. activators or prodn. stimulators in prevention and treatment of cardiovascular pathologies)

IT 89778-26-7, Toremifene 116057-66-0 116057-75-1, Idoxifene 116057-76-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(TGF-.beta. activators or prodn. stimulators in prevention and treatment of cardiovascular pathologies)

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (40) Wolf; US 4835002 1989 HCAPLUS
- (41) Wolinsky; US 4824436 1989

L79 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:404608 HCAPLUS

DN 127:60325

TI Coronary heart disease mortality and adjuvant **tamoxifen** therapy

AU Costantino, Joseph P.; Kuller, Lewis H.; Ives, Diane G.; Fisher, Bernard; Dignam, James

CS Department of Biostatistics, University of Pittsburgh, Pittsburgh, PA, 15261, USA

SO Journal of the National Cancer Institute (1997), 89(11), 776-782

CODEN: JNCIEQ; ISSN: 0027-8874

PB Oxford University Press

DT Journal

LA English

CC 1-6 (Pharmacology)

AB Data from randomized clin. trials in Scotland and Sweden testing the efficacy of **tamoxifen** therapy in patients with breast cancer have suggested that the drug may also reduce the risk of coronary heart disease. In view of these findings, the authors examd. mortality from coronary heart disease among patients with early stage breast cancer who were enrolled in the National Surgical Adjuvant Breast and Bowel Project B-14 trial of **tamoxifen** therapy. Deaths occurring among women who were randomly assigned to 5 yr of either **tamoxifen** or placebo in the first phase of the B-14 trial were reviewed to det. the cause. Three categories of heart disease-related death were defined: (1) death from a definite fatal myocardial infarction, (2) death from definite fatal coronary heart disease/possible myocardial infarction, and (3) death from possible fatal coronary heart disease. Comparisons of the findings by treatment group were made on the basis of av. annual hazard (i.e., death) rates and the corresponding relative hazard of death. The av. annual death rate from coronary heart disease was lower for patients who received **tamoxifen** than for patients who received placebo, but the difference was not statistically significant. There were eight definite heart-related deaths (i.e., definite fatal myocardial infarction or definite fatal coronary heart disease/possible myocardial infarction) among the patients who received **tamoxifen**, yielding an av. annual rate of 0.62 per 1000 patients. There were 12 definite heart-related deaths among the patients who received placebo, yielding an av. annual rate of 0.94 per 1000. The corresponding relative hazard of death from definite fatal heart disease (**tamoxifen** vs. placebo) was 0.66 (95% confidence interval = 0.27-1.61). Eleven deaths in the **tamoxifen** group and 10 deaths in the placebo group were classified as possible cases of fatal coronary heart disease. When these cases and the definite cases were considered together, the av. annual death rate for the patients who received **tamoxifen** was 1.48 per 1000, and the rate for the patients who received placebo was 1.73 per 1000. The corresponding relative hazard of death was 0.85 (95% confidence interval = 0.46-1.58). The findings from the B-14 trial are consistent with the findings from the Scottish and the Swedish trials, suggesting that **tamoxifen** treatment reduces coronary heart disease among patients with breast cancer. Continued follow-up of the patients in these trials and in ongoing prevention trials is needed to accumulate enough data so that reliable conclusions can be drawn about the benefits of **tamoxifen** in preventing heart disease.

ST coronary heart disease **tamoxifen** breast cancer; cancer antitumor

IT **Artery, disease**  
 (coronary; coronary heart disease mortality and adjuvant **tamoxifen** therapy in humans)

IT **Antitumor agents**  
 (mammary gland; coronary heart disease mortality and adjuvant **tamoxifen** therapy in humans)

IT **Mammary gland**  
 (neoplasm, inhibitors; coronary heart disease mortality and adjuvant **tamoxifen** therapy in humans)

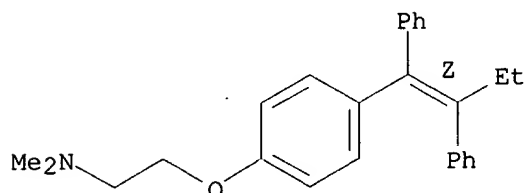
IT **10540-29-1, Tamoxifen**  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (coronary heart disease mortality and adjuvant **tamoxifen** therapy in humans)

IT **10540-29-1, Tamoxifen**  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (coronary heart disease mortality and adjuvant **tamoxifen** therapy in humans)

RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.



L79 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:134850 HCAPLUS

DN 126:139887

TI Prevention and treatment of cardiovascular pathologies with **tamoxifen** analogs

IN Grainger, David J.; Metcalfe, James C.; Kunz, Lawrence L.; Kemp, Paul R.; Schroff, Robert W.; Weissberg, Peter L.

PA Neorx Corporation, USA; Grainger, David J.; Metcalfe, James C.; Kunz, Lawrence L.; Kemp, Paul R.; Schroff, Robert W.; Weissberg, Peter L.

SO PCT Int. Appl., 130 pp.  
 CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-135

CC 1-8 (Pharmacology)

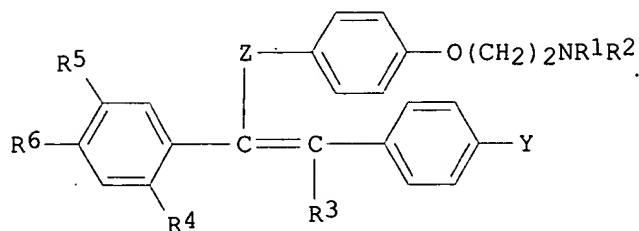
Section cross-reference(s): 63

FAN.CNT 14

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9640098	A2	19961219	WO 1996-US10211	19960607 <--
	WO 9640098	A3	19970619		
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,				



SE, SG  
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA  
 US 5595722 A 19970121 US 1995-476735 19950607 <--  
 US 5770609 A 19980623 US 1995-486334 19950607 <--  
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 AU 9662773 A1 19961230 AU 1996-62773 19960607 <--  
 EP 833624 A2 19980408 EP 1996-921577 19960607 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI  
 JP 11510479 T2 19990914 JP 1996-502239 19960607 <--  
 US 6197789 B1 20010306 US 1997-973570 19971205 <--  
 US 2002068731 A1 20020606 US 2001-754775 20010104 <--  
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 OS MARPAT 126:139887  
 GI



AB A method for treating or preventing cardiovascular pathologies comprises administering a compd. I (Z = C:O, covalent bond; Y = H, O(C1-4)alkyl; R1, R2 = (C1-4)alkyl, together with N satd. heterocyclic group; R3 = Et, chloroethyl; R4 = H; R5 = I, O(C1-4)alkyl, H; R6 = I, O(C1-C4)alkyl, H, with the proviso that when R4, R5, and R6 are H, R3 is not ethyl) or a pharmaceutically acceptable salt thereof, effective to elevate the level of TGF- $\beta$ . to treat and/or prevent conditions such as atherosclerosis, thrombosis, myocardial infarction, and stroke is provided. Useful compds. include idoxifene, raloxifene, toremifene, droloxifene or salts thereof. A method for identifying an agent that elevates the level of TGF- $\beta$  and an assay or kit to det. TGF- $\beta$ . based on anti-TGF- $\beta$ -antibodies are also provided. **Tamoxifen** (1.1 mg/kg/day) strongly inhibited the formation of lipid lesions induced by a high fat diet in mice. The major effect of **tamoxifen** in mice was to elevate TGF- $\beta$ . in aortic wall and in circulation.

ST **tamoxifen** analog cardiovascular disease; transforming growth factor beta **tamoxifen** analog

IT mRNA  
 RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)  
 (TGF- $\beta$ ., prodn. of, increase of; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)

IT DNA  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

- (adducts; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Antiarteriosclerotics
  - (antiatherosclerotics; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Medical goods
  - (catheters, for drug delivery to arterial lesion; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT **Artery**
  - Artery**
    - (coronary, angioplasty, drug delivery in; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Eye, disease
  - (diabetic retinopathy; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Heart, disease
  - (infarction, therapeutic agents; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Heart, disease
  - (infarction; **tamoxifen** analogs for prevention of cardiovascular diseases)
- IT **Blood vessel, disease**
  - (injury; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT **Artery, disease**
  - (lesions, drug delivery in; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Antibodies
  - RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
  - (monoclonal; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Proliferation inhibition
  - (proliferation inhibitors, vascular smooth muscle; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT **Blood vessel**
  - (smooth muscle, proliferation of, inhibition of; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Brain, disease
  - (stroke; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT **Blood vessel**
  - Blood vessel**
    - (surgery; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Drug delivery systems
  - (sustained-release; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Anticoagulants
  - Transplant and Transplantation
    - (**tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT Antibodies
  - RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
  - (**tamoxifen** analogs for prevention and treatment of cardiovascular diseases)
- IT **Atherosclerosis**
  - Thrombosis**
    - (**tamoxifen** analogs for prevention of cardiovascular diseases)
- IT Cell division
  - (vascular smooth muscle, inhibition of; **tamoxifen** analogs for

prevention and treatment of cardiovascular diseases)

IT Surgery  
Surgery  
(vascular; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)

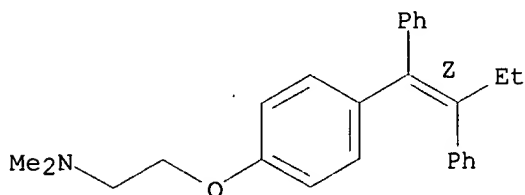
IT Transforming growth factors  
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)  
(.beta.-; **tamoxifen** analogs for prevention and treatment of cardiovascular diseases)

IT 10540-29-1, **Tamoxifen** 10540-29-1D,  
**Tamoxifen**, analogs 82413-20-5, Droloxifene 84449-90-1,  
Raloxifene 89778-26-7, Toremifene 116057-66-0 116057-75-1, Idoxifene 116057-76-2  
RL: BAC (Biological activity or effector, except adverse);  
BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**tamoxifen** analogs for prevention and treatment of cardiovascular diseases)

IT 10540-29-1, **Tamoxifen** 10540-29-1D,  
**Tamoxifen**, analogs  
RL: BAC (Biological activity or effector, except adverse);  
BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**tamoxifen** analogs for prevention and treatment of cardiovascular diseases)

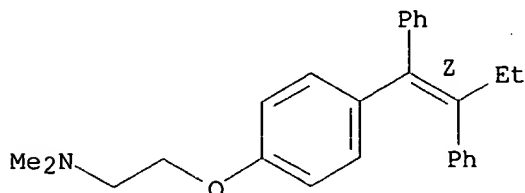
RN 10540-29-1 HCAPLUS  
CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



RN 10540-29-1 HCAPLUS  
CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



L79 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN  
AN 1996:126984 HCAPLUS  
DN 124:165616  
TI Effect of gender and sex steroids on the contractile response of canine coronary and renal blood vessels

AU Karanian, John W.; Ramwell, Peter W.  
 CS Lab. Membrane Biochem. Biophys., NIAAA, Washington, DC, USA  
 SO Journal of Cardiovascular Pharmacology (1996), 27(3), 312-19  
 CODEN: JCPCDT; ISSN: 0160-2446  
 PB Lippincott-Raven  
 DT Journal  
 LA English  
 CC 2-4 (Mammalian Hormones)  
 AB The effect of gender, gonadal steroids, and antiandrogen/antiestrogen-treatment on the isotonic response of isolated preps. of the left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX), and renal artery and vein of sexually mature dogs was investigated. The max. isotonic response of the coronary and renal vasculature to the thromboxane A2 (TXA2)-mimetic U46619 was significantly greater, and the EC50 value was significantly lower in males as compared with females. Moreover, similar gender differences in the contractile response of the coronary vasculature to **norepinephrine** were obsd. Pretreatment of male dogs with the antiandrogens flutamide or cyproterone acetate reduced the max. contractile response of the LAD to the TXA2-mimetic. Pretreatment of female dogs with testosterone resulted in an increase in both the max. contractile response and EC50 value to U46619. Antiestrogen treatment of female dogs with **tamoxifen** was assocd. with an increase in the max. contractile response of the LAD to U46619. Estrogen pretreatment of male dogs decreased both the max. contractile response and the EC50 value to U46619. Therefore, there is a sex difference in LAD and LCX contractile responses to both U46619 and **norepinephrine**. These results suggest that smooth muscle reactivity of dog coronary artery to the TXA2-mimetic U46619 may be susceptible to regulation by both androgens and estrogens. The obsd. gender differences in the catecholamine response may be similarly altered by changes in the hormonal milieu.

ST blood vessel heart kidney contraction gender; TXA2 heart kidney vessel sex steroid; **norepinephrine** heart kidney vessel sex steroid; androgen heart kidney vessel contraction; estrogen heart kidney vessel contraction

IT Sex  
 (gender and sex steroids effects on contractile response of canine coronary and renal blood vessels to **norepinephrine** and TXA2)

IT Androgens  
 Estrogens  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (gender and sex steroids effects on contractile response of canine coronary and renal blood vessels to **norepinephrine** and TXA2)

IT **Artery**  
 (coronary, gender and sex steroids effects on contractile response of canine coronary and renal blood vessels to **norepinephrine** and TXA2)

IT **Artery**  
**Vein**  
 (renal, gender and sex steroids effects on contractile response of canine coronary and renal blood vessels to **norepinephrine** and TXA2)

IT 51-41-2, **Norepinephrine** 58-22-0, Testosterone  
 313-06-4, Estradiol cypionate 427-51-0, Cyproterone acetate  
 10540-29-1, **Tamoxifen** 13311-84-7, Flutamide  
 56985-40-1, U-46619  
 RL: BAC (Biological activity or effector, except adverse);  
 BSU (Biological study, unclassified); BIOL (Biological study)  
 (gender and sex steroids effects on contractile response of canine coronary and renal blood vessels to **norepinephrine** and TXA2)

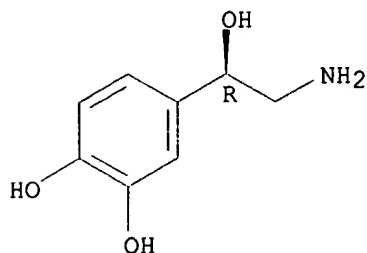
IT 51-41-2, **Norepinephrine** 10540-29-1,  
**Tamoxifen**

RL: BAC (Biological activity or effector, except adverse);  
 BSU (Biological study, unclassified); BIOL (Biological study)  
 (gender and sex steroids effects on contractile response of canine  
 coronary and renal blood vessels to **norepinephrine** and TXA2)

RN 51-41-2 HCAPLUS

CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

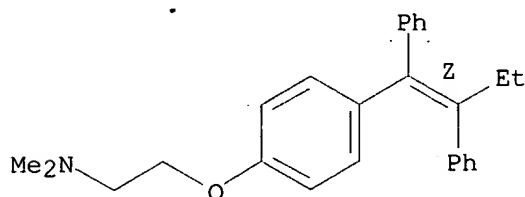
Absolute stereochemistry.



RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.



L79 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:13286 HCAPLUS

DN 124:45720

TI Method of treating peripheral vasoconstriction with **tamoxifen**  
 citrate

IN Stromberg, Brent V.

PA USA

SO U.S., 4 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-135

NCL 514648000

CC 1-8 (Pharmacology)

Section cross-reference(s): 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5470883	A	19951128	US 1994-247771	19940523 <--
PRAI	US 1994-247771		19940523 <--		

AB A method of modifying peripheral vasoconstriction comprises administering  
 a pharmacol. acceptable dose of a **tamoxifen** salt, e.g.  
**tamoxifen** citrate.

ST **tamoxifen** citrate peripheral vasoconstriction treatment

IT Adrenergic agonists

Blood vessel

(**tamoxifen** salts for treating peripheral

vasoconstriction)

IT 51-41-2, Norepinephrine 51-43-4, Epinephrine  
51-61-6, Dopamine, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(tamoxifen salts for treating peripheral vasoconstriction)

IT 54965-24-1, Tamoxifen citrate  
RL: BAC (Biological activity or effector, except adverse);  
BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tamoxifen salts for treating peripheral vasoconstriction)

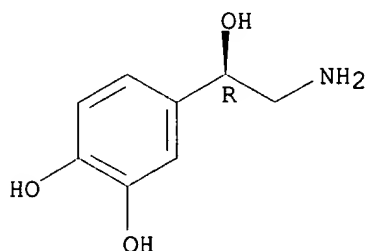
IT 10540-29-1D, Tamoxifen, salts  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tamoxifen salts for treating peripheral vasoconstriction)

IT 51-41-2, Norepinephrine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(tamoxifen salts for treating peripheral vasoconstriction)

RN 51-41-2 HCAPLUS

CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 54965-24-1, Tamoxifen citrate  
RL: BAC (Biological activity or effector, except adverse);  
BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tamoxifen salts for treating peripheral vasoconstriction)

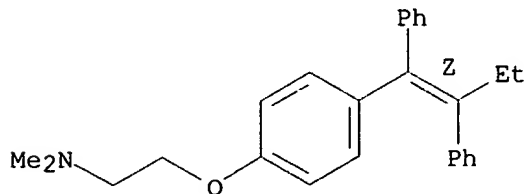
RN 54965-24-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl-,  
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 10540-29-1  
CMF C26 H29 N O

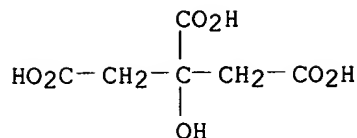
Double bond geometry as shown.



CM 2

CRN 77-92-9

CMF C6 H8 O7



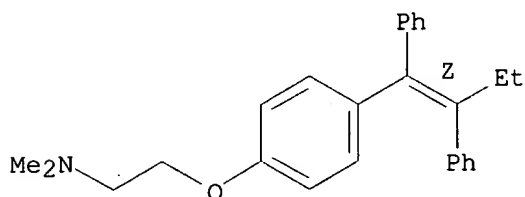
IT 10540-29-1D, Tamoxifen, salts

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tamoxifen salts for treating peripheral vasoconstriction)

RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



L79 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

AN 1985:154801 HCAPLUS

DN 102:154801

TI Prophylaxis and therapy for coronary heart diseases by lowering the  
estrogen level

IN Schulze, Paul Eberhard; Kerb, Ulrich

PA Schering A.-G. , Fed. Rep. Ger.

SO Ger. Offen., 9 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM A61K045-06

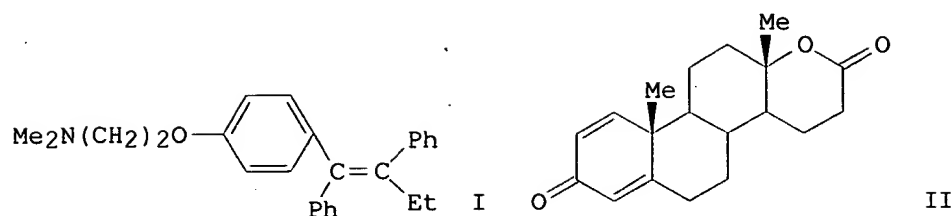
ICS A61K031-135; A61K031-12; A61K031-40; A61K031-565

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 3323321	A1	19850103	DE 1983-3323321	19830624	<--
	WO 8500107	A1	19850117	WO 1984-DE137	19840619	<--
	W: JP, US					
	RW: DE, FR, GB, NL					
	JP 60501656	T2	19851003	JP 1984-502536	19840619	<--
	EP 179062	A1	19860430	EP 1984-902507	19840619	<--
	R: DE, FR, GB, NL					
PRAI	DE 1983-3323321		19830624			<--
	WO 1984-DE137		19840619			<--
GI						



AB Coronary heart disease in men is treated by administration of an antiestrogen, such as **tamoxifen** (I) [10540-29-1], or an aromatase inhibitor, such as testololactone (II) [4416-57-3], in daily doses of 10-200 or 50-1000 mg, resp. Tablets were prepd. contg. II 100, lactose 80.5, cornstarch 39.5, PVP 2.5, Aerosil 2.0, and Mg stearate 0.5 mg.

ST coronary heart disease **tamoxifen** testololactone

IT **Heart, disease or disorder**  
(coronary, treatment of, with **tamoxifen** and testololactone pharmaceuticals in men)

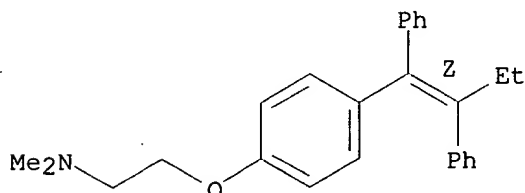
IT 4416-57-3 **10540-29-1**  
RL: BIOL (Biological study)  
(pharmaceuticals, for coronary heart disease treatment, in men)

IT **10540-29-1**  
RL: BIOL (Biological study)  
(pharmaceuticals, for coronary heart disease treatment, in men)

RN 10540-29-1 HCAPLUS

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



=> sel hit rn 179  
E40 THROUGH E42 ASSIGNED

=> fil reg  
FILE 'REGISTRY' ENTERED AT 10:48:50 ON 27 AUG 2003  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 25 AUG 2003 HIGHEST RN 573649-48-6  
DICTIONARY FILE UPDATES: 25 AUG 2003 HIGHEST RN 573649-48-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when



conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s e40-e42

1 10540-29-1/BI  
(10540-29-1/RN)

1 51-41-2/BI  
(51-41-2/RN)

1 54965-24-1/BI  
(54965-24-1/RN)

L80 3 (10540-29-1/BI OR 51-41-2/BI OR 54965-24-1/BI)

=> d ide can tot

L80 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2003 ACS on STN

RN 54965-24-1 REGISTRY

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl-,  
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Ethanamine, 2-[4-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethyl-, (Z)-,  
2-hydroxy-1,2,3-propanetricarboxylate (1:1)

OTHER NAMES:

CN I.C.I.46474 citrate

CN ICI 46474

CN Kessar

CN Noltam

CN Nolvadex

CN Nourytam

CN Tamofen

CN Tamoplex

CN Tamox-Puren

CN Tamoxifen citrate

CN TMX

CN Tomaxasta

CN Z-Tamoxifen citrate

CN Zemide

FS STEREOSEARCH

DR 7244-97-5

MF C26 H29 N O . C6 H8 O7

CI COM

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CAOLD, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,  
CSCHEM, DIOGENES, DRUGPAT, EMBASE, HSDB\*, IPA, MRCK\*, MSDS-OHS,  
PHARMASEARCH, PIRA, PROMT, RTECS\*, TOXCENTER, ULIDAT, USAN, USPATFULL  
(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

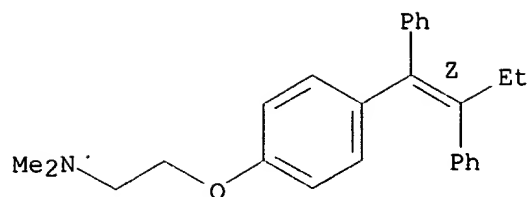
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

CM 1

CRN 10540-29-1

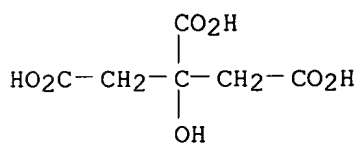
CMF C26 H29 N O

Double bond geometry as shown.



CM 2

CRN 77-92-9  
CMF C6 H8 O7



219 REFERENCES IN FILE CA (1937 TO DATE)  
219 REFERENCES IN FILE CAPLUS (1937 TO DATE)

REFERENCE 1: 139:101145  
REFERENCE 2: 139:101144  
REFERENCE 3: 139:101141  
REFERENCE 4: 139:79130  
REFERENCE 5: 139:63529  
REFERENCE 6: 139:47180  
REFERENCE 7: 139:30831  
REFERENCE 8: 139:12264  
REFERENCE 9: 138:406952  
REFERENCE 10: 138:395618

L80 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2003 ACS on STN

RN 10540-29-1 REGISTRY

CN Ethanamine, 2-[4-[(1Z)-1,2-diphenyl-1-butenyl]phenoxy]-N,N-dimethyl- (9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Ethanamine, 2-[4-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethyl-, (Z)-

CN Ethylamine, 2-[p-(1,2-diphenyl-1-butenyl)phenoxy]-N,N-dimethyl-, (Z)-  
(8CI)

OTHER NAMES:

CN ICI 47699

CN Mammaton

CN Tamoxifen

CN trans-Tamoxifen

CN Z-Tamoxifen

FS STEREOSEARCH

MF C26 H29 N O

CI COM

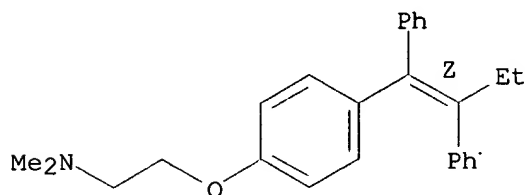
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, EMBASE, HSDB\*, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PROMT, RTECS\*, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5019 REFERENCES IN FILE CA (1937 TO DATE)

136 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

5032 REFERENCES IN FILE CAPLUS (1937 TO DATE)

REFERENCE 1: 139:131176

REFERENCE 2: 139:129670

REFERENCE 3: 139:129225

REFERENCE 4: 139:128591

REFERENCE 5: 139:128133

REFERENCE 6: 139:127969

REFERENCE 7: 139:127663

REFERENCE 8: 139:127602

REFERENCE 9: 139:127600

REFERENCE 10: 139:127537

L80 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2003 ACS on STN

RN 51-41-2 REGISTRY

CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,2-Benzenediol, 4-(2-amino-1-hydroxyethyl)-, (R)-

CN Benzyl alcohol, .alpha.-(aminomethyl)-3,4-dihydroxy-, (-)- (8CI)

OTHER NAMES:

CN (-)-.alpha.-(Aminomethyl)protocatechuyl alcohol

CN (-)-Arterenol

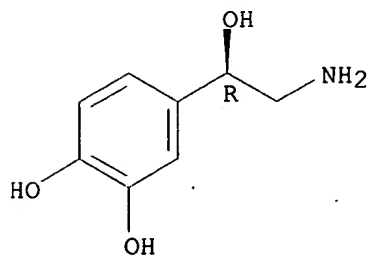
CN (-)-Noradrenaline

CN (-)-Norepinephrine

CN (R)-(-)-Norepinephrine

CN (R)-Noradrenaline  
 CN (R)-Norepinephrine  
 CN Adrenor  
 CN Aktamin  
 CN Arterenol  
 CN 1-.alpha.-(Aminomethyl)-3,4-dihydroxybenzyl alcohol  
 CN 1-1-(3,4-Dihydroxyphenyl)-2-aminoethanol  
 CN 1-2-Amino-1-(3,4-dihydroxyphenyl)ethanol  
 CN 1-3,4-Dihydroxyphenylethanolamine  
 CN 1-Arterenol  
 CN L-Noradrenaline  
 CN 1-Noradrenaline  
 CN 1-Norepinephrine  
 CN Levarterenol  
 CN Levóarterenol  
 CN Levonor  
 CN Levonoradrenaline  
 CN Levonorepinephrine  
 CN Levophed  
 CN Nor-Epirenan  
 CN Noradrenalin  
 CN Noradrenaline  
 CN Norartrinal  
 CN Norepinephrine  
 CN Norepirenamine  
 CN Sympathin E  
 FS STEREOSEARCH  
 DR 66197-73-7, 4899-05-2  
 MF C8 H11 N O3  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN\*, BIOBUSINESS,  
 BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB,  
 CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU,  
 DIOGENES, DRUGU, EMBASE, HODOC\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,  
 MRCK\*, MSDS-OHS, NAPRALERT, NIOSHTIC, PROMT, RTECS\*, SPECINFO,  
 SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

59111 REFERENCES IN FILE CA (1937 TO DATE)  
 258 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 59153 REFERENCES IN FILE CAPLUS (1937 TO DATE)  
 366 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:139915

REFERENCE 2: 139:133463  
REFERENCE 3: 139:132202  
REFERENCE 4: 139:131966  
REFERENCE 5: 139:131926  
REFERENCE 6: 139:131869  
REFERENCE 7: 139:131668  
REFERENCE 8: 139:131383  
REFERENCE 9: 139:131361  
REFERENCE 10: 139:131298

=> fil medline

FILE 'MEDLINE' ENTERED AT 11:02:24 ON 27 AUG 2003

FILE LAST UPDATED: 26 AUG 2003 (20030826/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l103 all tot

L103 ANSWER 1 OF 4 MEDLINE on STN

AN 2000108129 MEDLINE

DN 20108129 PubMed ID: 10643517

TI New aspects in Peyronie's disease--a mini-review.

AU Schroeder-Printzen I; Hauck E W; Weidner W

CS Department of Urology, Justus Liebig University, Giessen, Germany.

SO ANDROLOGIA, (1999) 31 Suppl 1 31-5. Ref: 28

Journal code: 0423506. ISSN: 0303-4569.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Priority Journals

EM 200002

ED Entered STN: 20000218

Last Updated on STN: 20000218

Entered Medline: 20000210

AB There have been several advances in elucidation of the pathogenesis of Peyronie's disease. Transforming growth factor beta 1 seems to play a major role in this disease, while the importance of penile trauma is a matter of debate. High-resolution ultrasound sonography is the method of choice in detecting penile plaques, while magnetic resonance imaging is useful in the evaluation of actively inflamed plaques. There are still differences of opinion on the best drug therapy in noncalcified plaques. The results on **tamoxifen** or interferon therapy vary between useless and useful. Potassium-para-aminobenzoate seems to have a significant effect in decreasing plaque size and deviation angle. The

operative strategy for big plaques or complex deviation has changed to the 'small incision' graft, leading to far lower post-operative impotence rates. Iontophoresis seems to be worthy of further trials, while the results of extracorporeal shock wave therapy have to be discussed critically.

CT Check Tags: Human; Male

Impotence: ET, etiology

\*Penile Induration

Penile Induration: DI, diagnosis

Penile Induration: ET, etiology

Penile Induration: TH, therapy

L103 ANSWER 2 OF 4 MEDLINE on STN

AN 2000034844 MEDLINE

DN 20034844 PubMed ID: 10569556

TI **Tamoxifen** versus placebo in the treatment of Peyronie's disease.

AU Teloken C; Rhoden E L; Grazziotin T M; Ros C T; Sogari P R; Souto C A

CS Department of Urology, Santa Casa Hospital and Fundacao Faculdade Federal de Ciencias Medicas, Porto Alegre, Brazil.

SO JOURNAL OF UROLOGY, (1999 Dec) 162 (6) 2003-5.

Journal code: 0376374. ISSN: 0022-5347.

CY United States

DT (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200001

ED Entered STN: 20000114

Last Updated on STN: 20000114

Entered Medline: 20000106

AB PURPOSE: We evaluated the effects of oral **tamoxifen** and placebo in patients with Peyronie's disease. MATERIALS AND METHODS: We selected 25 patients with Peyronie's disease who did not have calcified plaque for treatment in the andrology outpatient clinic. A medical history was obtained, and physical examination, penile x-ray, penile ultrasound and pharmacologically induced erection with prostaglandin E1 were performed. Patients were randomly divided into group 1--those who received 20 mg. **tamoxifen** twice daily for 3 months and group 2--those who received placebo for the same period. The same evaluations were done 4 months later and results were compared. Qualitative (chi-square test) and quantitative (Student's t test) results were analyzed using the Yates correction factor with  $p < 0.05$  considered significant. RESULTS: Pain subsided in 66.6 and 75% of the patients treated with **tamoxifen** and placebo, respectively ( $p > 0.05$ ). In groups 1 and 2 a reduction in the penile deformity was noticed by 46.1 and 41.7% of the patients ( $p > 0.05$ ), and a decrease in plaque size was noticed by 30.7 and 25%, respectively. On the other hand, objective measurements did not reveal any difference in plaque area or curvature angle. CONCLUSIONS: This study did not show significant improvement in pain, curvature or plaque size in patients with Peyronie's disease who were treated with **tamoxifen** compared with those treated with placebo.

CT Check Tags: Human; Male

Administration, Oral

Aged

Middle Age

\*Penile Induration: DT, drug therapy

\*Tamoxifen: AD, administration & dosage

RN 10540-29-1 (Tamoxifen)

L103 ANSWER 3 OF 4 MEDLINE on STN

AN 1998138816 MEDLINE

DN 98138816 PubMed ID: 9478329

TI The effect of **tamoxifen** on the neonatal development of rat glans penis.

AU Deveci E; Onen A; Tacar O; Yildirim A

CS Department of Histology and Embryology, Medical Faculty, University of Dicle, Diyarbakir, Turkiye.

SO CLINICAL AND EXPERIMENTAL OBSTETRICS AND GYNECOLOGY, (1997) 24 (4) 237-9.  
Journal code: 7802110. ISSN: 0390-6663.

CY Italy

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199803

ED Entered STN: 19980407  
Last Updated on STN: 19980407  
Entered Medline: 19980326

AB From the first day of birth to the fifth day, daily subcutaneous 100 micrograms **tamoxifen** (Tx) was injected into new-born male rats. The penises that were taken totally were fixated in 10% formaline, and then they were put in paraffin inclusion. The paraffin sections were stained with Hematoxylen-Eosin, Verhoeff and Triple on days 7, 14, 21, 28, 35 and 60. The alterations in the development of glans penis construction were examined. We found that in the glans penis of animals which were given Tx, from the 21st day, the epidermal projections were erased slowly and on the 60th day the epidermal projections and keratinisation completely ceased altogether. As a result, the development of epidermal projections in rats which were given **tamoxifen** in the neonatal period were hindered.

CT Check Tags: Animal; Male  
\*Animals, Newborn  
Atrophy  
\*Epidermis: DE, drug effects  
\*Epidermis: GD, growth & development  
Epidermis: PA, pathology  
Epithelium: DE, drug effects  
Epithelium: PA, pathology  
\*Estrogen Antagonists: PD, pharmacology  
Injections, Subcutaneous  
Keratin: ME, metabolism  
\*Penis: DE, drug effects  
\*Penis: GD, growth & development  
Rats  
Tamoxifen: AD, administration & dosage  
\*Tamoxifen: PD, pharmacology

RN 10540-29-1 (Tamoxifen); 68238-35-7 (Keratin)

CN 0 (Estrogen Antagonists)

L103 ANSWER 4 OF 4 MEDLINE on STN

AN 93136902 MEDLINE

DN 93136902 PubMed ID: 1486392

TI The treatment of Peyronie's disease with **tamoxifen**.

AU Ralph D J; Brooks M D; Bottazzo G F; Pryor J P

CS St Peter's Hospitals, London.

SO BRITISH JOURNAL OF UROLOGY, (1992 Dec) 70 (6) 648-51.  
Journal code: 15740090R. ISSN: 0007-1331.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199302

ED Entered STN: 19930312  
Last Updated on STN: 19930312  
Entered Medline: 19930224

AB This is a preliminary study of the treatment of 36 patients with Peyronie's disease who received **tamoxifen** 20 mg twice daily for 3 months. An improvement occurred in 16 of 20 patients with penile pain, in 11 of 31 patients with an erectile deformity and 12 of 35 patients had a plaque shrinkage of at least 1 cm. Some improvement occurred in 6 of the 8 patients with a histologically confirmed inflammatory infiltrate of the plaque but not in any of the 4 patients without an infiltrate. The inflammatory infiltrate was found in patients in whom the duration of the disease was less than 4 months.

CT Check Tags: Human; Male  
Adult  
Aged  
Middle Age  
\*Penile Induration: DT, drug therapy  
Penile Induration: PA, pathology  
Penis: PA, pathology  
\*Tamoxifen: TU, therapeutic use  
Time Factors

RN 10540-29-1 (Tamoxifen)

=> d all tot

L109 ANSWER 1 OF 2 MEDLINE on STN  
AN 2000238189 MEDLINE  
DN 20238189 PubMed ID: 10775130  
TI Endothelium modulates anion channel-dependent aortic contractions to iodide.  
AU **Lamb F S**; Barna T J  
CS Department of Pediatrics, University of Iowa, Iowa City, Iowa 52242, USA..  
fred-lamb@uiowa.edu  
NC HL-62483 (NHLBI)  
SO AMERICAN JOURNAL OF PHYSIOLOGY. HEART AND CIRCULATORY PHYSIOLOGY, (2000 May) 278 (5) H1527-36.  
Journal code: 100901228. ISSN: 0363-6135.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200006  
ED Entered STN: 20000706  
Last Updated on STN: 20000706  
Entered Medline: 20000628

AB Anion currents contribute to vascular smooth muscle (VSM) membrane potential. The substitution of extracellular chloride (Cl) with iodide (I) or bromide (Br) initially inhibited and then potentiated isometric contractile responses of rat aortic rings to norepinephrine. Anion substitution alone produced a small relaxation, which occurred despite a lack of active tone and minimal subsequent contraction of endothelium-intact rings (4.2 +/- 1.2% of the response to 90 mM KCl). Endothelium-denuded rings underwent a similar initial relaxation but then contracted vigorously (I > Br). Responses to 130 mM I (93.7 +/- 1.9% of 90 mM KCl) were inhibited by nifedipine (10(-6) M), niflumic acid (10(-5) M), **tamoxifen** (10(-5) M), DIDS (10(-4) M), and HCO(-)(3)-free buffer (HEPES 10 mM) but not by bumetanide (10(-5) M). Intact rings treated with N(omega)-nitro-L-arginine (10(-4) M) responded weakly to I (15.5 +/- 2.1% of 90 mM KCl), whereas hemoglobin (10(-5) M), indomethacin (10(-6) M), 17-octadecynoic acid (10(-5) M), and 1H-[1,2,4]oxadiazole[4,3-a]quinoxalin-1-one (10(-6) M) all failed to augment the response of intact rings to I. We hypothesize that VSM takes up I primarily via an anion exchanger. Subsequent I efflux through anion channels having a selectivity of I > Br > Cl produces depolarization. In endothelium-denuded or agonist-stimulated vessels, this current is



sufficient to activate voltage-dependent calcium channels and cause contraction. Neither nitric oxide nor prostaglandins are the primary endothelial modulator of these anion channels. If they are regulated by an endothelium-dependent hyperpolarizing factor it is not a cytochrome P-450 metabolite.

CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

**Aorta: DE, drug effects**

**\*Aorta: ME, metabolism**

Bromides: PD, pharmacology

Calcium Channel Blockers: PD, pharmacology

Chloride Channels: AI, antagonists & inhibitors

Dose-Response Relationship, Drug

**\*Endothelium, Vascular: ME, metabolism**

Enzyme Inhibitors: PD, pharmacology

Ion Channels: DE, drug effects

\*Ion Channels: ME, metabolism

Ion Transport: DE, drug effects

Nifedipine: PD, pharmacology

Norepinephrine: PD, pharmacology

Potassium Chloride: PD, pharmacology

Rats

Rats, Sprague-Dawley

Sodium Chloride: PD, pharmacology

Sodium Compounds: PD, pharmacology

\*Sodium Iodide: PD, pharmacology

Sulfuric Acid Esters: PD, pharmacology

**Vasoconstriction: DE, drug effects**

**\*Vasoconstriction: PH, physiology**

RN 21829-25-4 (Nifedipine); 51-41-2 (Norepinephrine); 7447-40-7 (Potassium Chloride); 75-93-4 (methyl sulfate); 7647-14-5 (Sodium Chloride); 7647-15-6 (sodium bromide); 7681-82-5 (Sodium Iodide)

CN 0 (Bromides); 0 (Calcium Channel Blockers); 0 (Chloride Channels); 0 (Enzyme Inhibitors); 0 (Ion Channels); 0 (Sodium Compounds); 0 (Sulfuric Acid Esters)

L109 ANSWER 2 OF 2 MEDLINE on STN

AN 1998355830 MEDLINE

DN 98355830 PubMed ID: 9688908

TI Chloride ion currents contribute functionally to norepinephrine-induced vascular contraction.

AU **Lamb F S**; Barna T J

CS Department of Pediatrics, University of Iowa, Iowa City, Iowa, 52242, USA.

NC P30-HD-27748 (NICHD)

SO AMERICAN JOURNAL OF PHYSIOLOGY, (1998 Jul) 275 (1 Pt 2) H151-60.

Journal code: 0370511. ISSN: 0002-9513.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199808

ED Entered STN: 19980903

Last Updated on STN: 19980903

Entered Medline: 19980827

AB Norepinephrine (NE) increases Cl<sup>-</sup> efflux from vascular smooth muscle (VSM) cells. An increase in Cl<sup>-</sup> conductance produces membrane depolarization. We hypothesized that if Cl<sup>-</sup> currents are important for agonist-induced depolarization, then interfering with cellular Cl<sup>-</sup> handling should alter contractility. Isometric contraction of rat aortic rings was studied in a bicarbonate buffer. Substitution of extracellular Cl<sup>-</sup> with 130 mM methanesulfonate (MS; 8 mM Cl<sup>-</sup>) did not cause contraction. NE- and serotonin-induced contractions were potentiated in this low-Cl<sup>-</sup> buffer, whereas responses to K<sup>+</sup>, BAY K 8644, or NE in the absence of Ca<sup>2+</sup> were

unaltered. Substitution of Cl<sup>-</sup> with I<sup>-</sup> or Br<sup>-</sup> suppressed responses to NE. Inhibition of Cl<sup>-</sup> transport with bumetanide (10<sup>-5</sup> M) or bicarbonate-free conditions (10 mM HEPES) inhibited NE- but not KCl-induced contraction. The Cl<sup>-</sup>-channel blockers DIDS (10<sup>-3</sup> M), anthracene-9-carboxylic acid (10<sup>-3</sup> M), and niflumic acid (10<sup>-5</sup> M) all inhibited NE-induced contraction, whereas **tamoxifen** (10<sup>-5</sup> M) did not. Finally, disruption of sarcoplasmic reticular function with cyclopiazonic acid (10<sup>-7</sup> M) or ryanodine (10<sup>-5</sup> M) prevented the increase in the peak response to NE produced by low-Cl<sup>-</sup> buffer. We conclude that a Cl<sup>-</sup> current with a permeability sequence of I<sup>-</sup> > Br<sup>-</sup> > Cl<sup>-</sup> > MS is critical to agonist-induced contraction of VSM.

CT Check Tags: Animal; In Vitro; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

4,4'-Diisothiocyanostilbene-2,2'-Disulfonic Acid: PD, pharmacology

Anions: ME, metabolism

Anthracenes: PD, pharmacology

**Aorta, Thoracic: DE, drug effects**

**\*Aorta, Thoracic: PH, physiology**

Bay-K-8644: PD, pharmacology

Bicarbonates: PD, pharmacology

Cell Membrane Permeability

Chloride Channels: AI, antagonists & inhibitors

\*Chloride Channels: PH, physiology

\*Chlorides: PD, pharmacology

Indoles: PD, pharmacology

Isometric Contraction: DE, drug effects

\*Isometric Contraction: PH, physiology

Mesylates: PD, pharmacology

**Muscle, Smooth, Vascular: DE, drug effects**

**\*Muscle, Smooth, Vascular: PH, physiology**

Niflumic Acid: PD, pharmacology

\*Norepinephrine: PD, pharmacology

Potassium: PD, pharmacology

Rats

Rats, Sprague-Dawley

Ryanodine: PD, pharmacology

Sarcoplasmic Reticulum: DE, drug effects

Sarcoplasmic Reticulum: PH, physiology

Serotonin: PD, pharmacology

**Vasoconstriction: DE, drug effects**

**\*Vasoconstriction: PH, physiology**

Vasodilator Agents: PD, pharmacology

RN 15662-33-6 (Ryanodine); 18172-33-3 (cyclopiazonic acid); 4394-00-7 (Niflumic Acid); 50-67-9 (Serotonin); 51-41-2 (Norepinephrine); 53005-05-3 (4,4'-Diisothiocyanostilbene-2,2'-Disulfonic Acid); 71145-03-4 (Bay-K-8644); 723-62-6 (9-anthroic acid); 7440-09-7 (Potassium); 75-75-2 (methanesulfonic acid)

CN 0 (Anions); 0 (Anthracenes); 0 (Bicarbonates); 0 (Chloride Channels); 0 (Chlorides); 0 (Indoles); 0 (Mesylates); 0 (Vasodilator Agents)

=> fil biosis

FILE 'BIOSIS' ENTERED AT 11:05:44 ON 27 AUG 2003

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FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 20 August 2003 (20030820/ED)

=> d all

L117 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
AN 1999:170544 BIOSIS  
DN PREV199900170544  
TI **Tamoxifen** normalizes the increase in vascular sensitivity  
associated with endothelial disruption.  
AU Liu, B.-X.; Barna, T. J.; Lamb, F. S.  
CS Univ. Iowa Pediatr., Iowa City, IA 52242 USA  
SO FASEB Journal, (March 12, 1999) Vol. 13, No. 4 PART 1, pp. A59.  
Meeting Info.: Annual Meeting of the Professional Research Scientists for  
Experimental Biology 99 Washington, D.C., USA April 17-21, 1999  
ISSN: 0892-6638.  
DT **Conference**  
LA English  
CC Pharmacology - Cardiovascular System \*22010  
Biophysics - Membrane Phenomena \*10508  
Metabolism - Minerals \*13010  
Cardiovascular System - Blood Vessel Pathology \*14508  
Pharmacology - Drug Metabolism; Metabolic Stimulators \*22003  
Pharmacology - Endocrine System \*22016  
General Biology - Symposia, Transactions and Proceedings of Conferences,  
Congresses, Review Annuals \*00520  
Biochemical Studies - Sterols and Steroids \*10067  
Biochemical Studies - Minerals \*10069  
External Effects - Physical and Mechanical Effects \*10612  
Endocrine System - Gonads and Placenta \*17006  
Laboratory Animals - General \*28002  
In Vitro Studies, Cellular and Subcellular \*32600  
BC Muridae 86375  
IT Major Concepts  
Cardiovascular System (Transport and Circulation); Pharmacology  
IT Parts, Structures, & Systems of Organisms  
aorta: circulatory system, endothelial disruption-induced sensitivity,  
**tamoxifen** normalization  
IT Chemicals & Biochemicals  
**tamoxifen**: cardiovascular - drug, chloride ion current  
inhibitor  
IT Miscellaneous Descriptors  
Meeting Abstract  
ORGN Super Taxa  
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia  
ORGN Organism Name  
rat (Muridae): animal model  
ORGN Organism Superterms  
Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates;  
Rodents; Vertebrates  
RN 10540-29-1 (**TAMOXIFEN**)  
16887-00-6 (CHLORIDE ION)

=> d his

(FILE 'HOME' ENTERED AT 09:47:43 ON 27 AUG 2003)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:48:08 ON 27 AUG 2003

L1 2 S US20020065325/PN OR (WO2002-US26120# OR WO2000-US4892# OR US2  
SEL RN

FILE 'REGISTRY' ENTERED AT 09:50:12 ON 27 AUG 2003

L2 17 S E1-E17

L3 1 S L2 AND C26H29NO

L4 109 S C26H29NO/MF AND 46.150.18/RID AND 3/NR  
 L5 24 S L4 AND BUTEN? AND PHENOXY AND DIMETHYL AND ETHANAMINE  
 L6 5 S L5 NOT (LABELED OR (D OR T)/ELS OR 14C#)  
 L7 4 S L6 NOT 2 BUTENYL  
 L8 4 S L3,L7  
 SEL RN  
 L9 24 S E18-E21/CRN  
 L10 14 S L9 NOT (COMPD OR WITH OR MXS/CI)  
 L11 18 S L8,L10  
 L12 STR  
 L13 18 S L12 CSS SAM  
 L14 SCR 2039 OR 2043 OR 2054  
 L15 16 S L12 NOT L14 CSS  
 L16 422 S L12 NOT L14 CSS FUL  
 SAV L16 JKIM930/A  
 L17 STR L12  
 L18 11 S L17 CSS SAM SUB=L16  
 L19 4 S L16 AND C6-C6/ES  
 L20 235 S L17 CSS FUL SUB=L16  
 SAV L20 JKIM930A/A  
 L21 182 S L20 AND 3/NR  
 L22 35 S L20 AND 4/NR  
 L23 18 S L20 NOT L11,L21,L22  
 L24 9 S L23 NOT (NC5/ES OR CLO4 OR MXS/CI OR C60H66N4O4 OR C20H8BR4O5)

FILE 'HCAPLUS' ENTERED AT 10:14:03 ON 27 AUG 2003

L25 5223 S L11  
 L26 7288 S TAMOXIFEN# OR ICI47699 OR ICI() (47699 OR 47 699)  
 L27 5795 S L19 OR L21 OR L22 OR L24  
 L28 7816 S L25-L27  
 E BLOOD VESSEL/CT  
 L29 65303 S E3-E59  
 L30 13171 S E60-E96  
 L31 6190 S E109-E115  
 E E3+ALL  
 L32 143069 S E5,E4+NT  
 E E25+ALL  
 L33 92479 S E4,E5,E3+NT  
 E E114+ALL  
 E E28+ALL  
 L34 4260 S E3  
 E E8+ALL  
 E E30+ALL  
 L35 5383 S E3  
 E E10+ALL  
 L36 9115 S E4  
 E IMPOTENCE/CT  
 E E3+ALL  
 L37 1385 S E2  
 E ERECT/CT  
 E E10+ALL  
 E PENI/CT  
 E PENIL/CT  
 E E7+ALL  
 L38 446 S E2  
 E PENIS/CT  
 L39 1507 S E3-E8  
 E E3+ALL  
 L40 1902 S E6+NT  
 L41 324 S L28 AND L29-L40  
 L42 177 S L41 AND (PD<=19990226 OR PRD<=19990226 OR AD<=19990226)  
 L43 121 S L42 AND L25  
 L44 125 S L42 AND L27

L45 125 S L43,L44  
L46 52 S L42 NOT L45  
L47 2 S L46 AND (NOREPINEPHRIN? OR CARDIOVASCULAR PATHOLOG?)/TI  
E LAMB F/AU  
L48 7 S E3,E11  
L49 22 S E29,E31  
E SCHUTTE B/AU  
L50 57 S E3,E4,E7-E9  
E YANG B/AU  
L51 787 S E3-E24  
E YANG BAO/AU  
L52 18 S E3  
L53 21 S E60  
L54 4 S L28 AND L48-L53  
L55 92 S L45 AND (PHARMACOL? OR PHARMACEUT?)/SC,SX  
L56 2386 S (L11 OR L19 OR L21 OR L22 OR L24) (L)THU/RL  
L57 551 S (L11 OR L19 OR L21 OR L22 OR L24) (L) (DMA OR PAC OR PKT)/RL  
L58 2620 S (L11 OR L19 OR L21 OR L22 OR L24) (L) (BAC OR BCP OR BPR OR BSU  
L59 104 S L45 AND L56-L58  
L60 119 S L55,L59  
L61 6 S L45 NOT L60  
SEL L60 DN AN 3 8 9 27 74 81 93 119  
L62 8 S L60 AND E1-E24  
L63 11 S L1,L47,L54,L62 AND L25-L62  
L64 4 S L63 AND (CL OR CL3 OR CLC3) (L)CHANNEL?  
L65 3 S L63 AND (CHANNEL OR ION OR CHLORIDE OR CHLORIN?) (L)BLOCK?  
L66 4 S L64,L65  
L67 4 S L63 AND CHLORIDE (L)CHANNEL  
L68 4 S L66,L67

FILE 'REGISTRY' ENTERED AT 10:43:58 ON 27 AUG 2003

L69 1 S NOREPINEPHRINE/CN  
L70 5 S C8H11NO3/MF AND NOREPINEPHRIN?  
L71 3 S L70 NOT LABELED  
L72 3 S L69,L71

FILE 'HCAPLUS' ENTERED AT 10:45:21 ON 27 AUG 2003

L73 27 S L72 AND L28  
L74 19 S NOREPINEPHRIN? AND L28  
L75 10 S L73,L74 AND L42  
SEL DN AN 3 5 8 9 10  
L76 5 S L75 NOT E25-E39  
L77 6 S L68,L76  
L78 6 S L63 NOT L77  
L79 12 S L77,L78 AND L1,L25-L68,L73-L78

FILE 'REGISTRY' ENTERED AT 10:48:11 ON 27 AUG 2003

FILE 'HCAPLUS' ENTERED AT 10:48:33 ON 27 AUG 2003  
SEL HIT RN L79

FILE 'REGISTRY' ENTERED AT 10:48:50 ON 27 AUG 2003

L80 3 S E40-E42

FILE 'MEDLINE' ENTERED AT 10:49:16 ON 27 AUG 2003

L81 9336 S L11  
L82 11681 S L26  
L83 9336 S L27  
L84 8664 S L81-L83 AND PY<=1999  
E IMPOTENCE/CT  
E E3+ALL  
L85 8306 S E12+NT  
E E11+ALL

L86 3462 S E PENIL/CT  
 E E44+ALL  
 L87 9608 S E5+NT  
 E PENILE/CT  
 E E8+ALL  
 L88 22633 S E4+NT  
 E PENIS/CT  
 E E3+ALL  
 L89 15145 S E5+NT  
 E VASODILAT/CT  
 E E5+ALL  
 L90 15236 S E5+NT  
 E VASOCONSTRICT/CT  
 E E4+ALL  
 L91 4751 S E5+NT  
 E DIABETES/CT  
 E E4+ALL  
 L92 160300 S E13+NT  
 E DIABETES M/CT  
 E E4+ALL  
 L93 159681 S E6+NT  
 E HYPERTENSION/CT  
 E E3+ALL  
 L94 171519 S E4+NT  
 E BLOOD PRESSURE/CT  
 E E3+ALL  
 L95 8424 S E5+NT  
 E CORONARY ARTERY/CT  
 E E28+ALL  
 E E2+ALL  
 L96 131079 S E15+NT  
 E E14+ALL  
 L97 830845 S E9+NT  
 E VASCULAR/CT  
 E E208+ALL  
 E E7+ALL  
 L98 407473 S E3+NT  
 E VASULATURE/CT  
 E VASCULATURE/CT  
 E VASCULAR TISSUE/CT  
 E E4+ALL  
 E ARTERIES/CT  
 E E3+ALL  
 E E3+ALL  
 L99 59462 S E3+NT  
 L100 10 S E103+NT  
 L101 249 S L84 AND L85-L88  
 L102 0 S L84 AND L89-L99  
 L103 4 S L100 AND L101  
 L104 55 S L100 AND L101  
 L105 194 S L100 AND L101  
 L106 98 S L100 AND L101  
 SEL DN AN L100 1-3 5  
 L107 3 S L100 AND E1-E12  
 L108 2 S L101 NOT AB/FA  
 L109 2 S L101 NOT L104  
 L110 58 S L105 NOT C4./CT

FILE 'MEDLINE' ENTERED AT 11:02:24 ON 27 AUG 2003

L107 3 S L81-L83 AND (LAMB F? OR SCHUTTE B? OR YANG B?)/AU  
 L108 2 S L107 NOT APOPTOSIS  
 L109 2 S L108 AND L81-L106

FILE 'BIOSIS' ENTERED AT 11:03:44 ON 27 AUG 2003

E LAMB F/AU  
 L110 58 S E3,E10,E12,E14

L111           E SCHUTTE B/AU  
179 S E3,E4,E7-E10  
E YANG B/AU  
L112           533 S E3-E25  
E YAND BAO/AU  
E YANG BAO/AU  
L113           17 S E19  
L114           766 S L110-L113  
L115           11884 S L28  
L116           3 S L114 AND L115  
L117           1 S L116 AND CONFERENCE/DT

FILE 'BIOSIS' ENTERED AT 11:05:44 ON 27 AUG 2003